REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claims 87, 93, 94 and 97 are currently being amended.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 87, 93-95, 97-100, 111, 113, 116 and 141-144 are now pending in this application.

Applicant notes that the Advisory Action recites Claims 137-140 as still pending in the application. However, all of these claims were cancelled in Paper 34, at page 3 thereof (Amendment of February 9, 2003). Confirmation of the cancellation of these claims is therefore requested.

As the Advisory Action appears to maintain the rejections of the pending claims made in the Final Office Action of April 22, 2003 (Paper 35), reference in the remarks below is made to the text of that Action.

B. Response to Rejections Under Section 112, First Paragraph, Re "Murine" Domains

At pages 3 and 7 of the Office Action, the claims are rejected on the basis that the disclosure does not support claims to use of ligand encoding domains from murine species other than the mouse. Without conceding the basis of the rejection, and for the purpose of expediting prosecution, the claims have been amended to recite that the source of the murine component of the molecules is the mouse.

Reconsideration and withdrawal of the rejections is therefore respectfully requested.

C. Response to Rejection Under Section 112, First Paragraph, re "One or More Domains"

At page 3 of the Office Action, the claims are rejected for lack of written description with respect to the presence of "one or more" ligand domains from human and/or mouse sources within the molecules whose use is claimed.

Applicant respectfully disagrees. Support for the "one or more" limitation, as used in reference to the domain elements included in the chimeric molecules, is found at various places within the Specification, including:

a) Original Claims 1-10 were directed to molecules in which the base molecule having specified domains have one or more additional domains. For example, original Claims 9-10, now cancelled, read as follows (emphasis added):

> 9. The isolated polynucleotide sequence of claim 1 or claim 2 wherein the first nucleotide sequence encodes domains I, II and III, or subdomains of **one or more** of domains I, II and III, of a tumor necrosis factor ligand selected from the group consisting of CD154, CD70, Fas ligand, and TRAIL and the second nucleotide sequence encodes domain IV, or a subdomain of domain IV, of native TNFα.
>
> 10. The isolated polynucleotide sequence of claim 9 wherein the first nucleotide sequence encodes domains I, II and III, or subdomains of **one or more** domains I, II and III, of CD154 and the second nucleotide sequence encodes domain IV, or a subdomain of domain IV, of native TNFα.

b) Further, paragraphs 34 and 35 at page 9; paragraph 084 at page 20, and paragraph 086 at page 21 all recite embodiments in which one domain, or one or more domains (individually or in combination), are included in the chimeric molecule. For example, paragraph 084 at page 20 reads as follows (emphasis added):

> Thus, this first sequence may, without limitation, encode any of the following **domains, subdomains or combinations thereof**: a subdomain of domain III replacing a cleavage site of native TNFα; all of domain III; domain III with domain II or a subdomain thereof replacing a native TNFα cleavage site; domain III with domain I or a subdomain thereof replacing a native TNFα cleavage site; domain III with a subdomain of domain IV replacing a native TNFα cleavage site; domain III, domain II and domain I, or subdomains thereof. Preferably, the first nucleotide sequence encodes **at least one domain or subdomain of one of the following TNF ligands:** CD154, CD70, FasL and TRAIL. According to the invention, replacing a domain or subdomain containing a TNFα cleavage site with a domain or subdomain from one of these four other TNF ligands results in a chimeric TNFα that is markedly less susceptible to cleavage than native TNFα.

Thus, Applicant respectfully submits that the recited limitation directed to inclusion of one or more of the ligand domains within the chimeric molecule is fully supported by the Specification. Reconsideration and withdrawal of the claims rejection is therefore requested.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Atty. Dkt. No. 041673-2069

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

Date 3-23-04

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